accumulation of collagen, increased levels of connective tissue growth factor, transforming growth factor β1, tumor necrosis factor-alpha, vascular cell adhesion molecule 1, 3-nitrotyrosine and 4-hydroxy-2-nonenal in the aorta.
Conclusions: These findings suggested that chronic IH may lead to aortic damages characterized by oxidative stress and inflammation, and MT may play a pivotal role in the above pathogenesis process.

GW25-e0790

Effects of (P) RR and PLC-beta3 activation on cardiac hypertrophy in hypertensive rats

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Objectives: (Pro) renin receptor (P) RR, a newly identified member of the renin-angiotensin system, is a promising novel drug target because of its crucial involvement in renal and cardiac end-organ damage, but the mechanism of (P) RR on the end-organ damage remains unclear so far. Recently, some findings support the (pro) renin-(P) RR interaction at exceptionally high (pro) renin levels in vitro. However, the conflicting resutls obtained with handle region peptide (HRP) in vivo and invitro argue against the idea that this drug truly blocks the (pro) renin-(P) RR interaction in the intact animals. In this study, we investigated the role of cardiac (P) RR activation on the expression of PLC-beta3, PKC and ERK1/2 and on cardiac hypertrophy in hypertensive rats with abdominal aortic ligation.
Methods: Seventy-five SD rats were divided into 5 groups (n=15 each group) as following: sham operated (SO), rats with the aortic ligation (AL), AL rats were given HRP (4ug kg^{-1} d^{-1}, SC), AL rats given U73122 (40ug kg^{-1} d^{-1}, SC) and AL rats given HRP+U73122. MAP was recorded using a tail-cuff method. After 4 weeks of treatment, levels of (P) RR, PLC-beta3, PKC-a and ERK1/2 in the heart were examined by RT-PCR and western blot. The surface area of cardiomyocytes was measured.
Results: The expressional levels of (P) RR and PLC-beta3 significantly increased in the left ventricle in hypertensive rats ($P<0.01$, respectively). The surface area of cardiomyocytes and MAP rose markedly ($P<0.01$). HRP treatment significantly reduced the expression of (P) RR and U73122 suppressed the level of PLC-beta3. The combined treatment of HRP and U73122 significantly decreased levels of PKC-a and ERK1/2 in the heart ($P<0.01$). Meanwhile, the surface area of cardiomyocytes and MAP were decreased after the treatment ($P<0.01$).
Conclusions: This is the first report demonstrating that treatment of HRP and U73122 decreased levels of (P) RR, PLC-beta3, PKC-a and ERK1/2 in the heart. Meanwhile, the treatment reduced the surface area of cardiomyocytes and MAP. These findings indicate that cardiac (P) RR may activate PLC-beta3, PKC and ERK1/2 signals and result in hypertension and cardiac hypertrophy.

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GW25-e0850

Effect of acute high altitude exposure on lung function and relationship between lung function and AMS

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Objectives: To investigate the effect of acute high altitude exposure on lung function and the relationship between lung function and AMS.
Methods: we collected the lung function and Lewis Lake data of 73 subjects (age 18 to 26, male) at sea-leve and junmachang (after five days Exposure to 3000m, 3900m).
Results: compared with sea-leve, lung function decreased in FVC, MMF, V50, V25 While FEV1, PEF, V75 did not change; FVC, FEV1, PEF, MMF was used to analyze the relationship between lung function and AMS, there is No differe-nces in lung function between AMS group and NON AMS group at sea-leve, lung function of AMS group is statistically significant lower than NON AMS group in FVC, MMF at high altitude; there is differences between AMS group and NON AMS group in the rate of change of FVC, MMF; logistic regression analysis showed that the rate of change of the FVC was independent risk factors, correlation analysis showed that the change of FVC and the change of oxygen saturation is relative.
Conclusions: lung function showed restriction decreased after acute high altitude exposure, the changes of lung function will increase the hypoxia and susceptible AMS.

GW25-e0876

Role of GRK4γ variant 142V in the regulation of renal ETB receptor in hypertension

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Objectives: The endothelin receptor B (ETBR) regulates blood pressure and water and electrolyte balance by engendering natriuresis. In hypertensive states, the ETBR mediated diureis and natriuresis is impaired. However, the underlying mechanisms are not clear. G protein-coupled receptor kinase 4 (GRK4), whose gene locus 4p16.3 is linked to essential hypertension, cause sodium retention and increase blood pressure via impairment of renal dopamine receptor and enhancement of renin-angiotensin system functions. Due to the higher activity of GRK4 in kidney from spontaneously hypertensive rats (SHRs) and hypertensive patients, we hypothesize that GRK4 might be the cause of ETBR impairment in hypertension.
Methods: Experiments were carried out in male anaesthetic spontaneously hypertensive rats (SHR) and in normotensive Wistar-Kyoto (WKY) rats. The ETB receptor agonist, BQ-3020 (0.1,0.5,1.0ug/kg/min) were infused via supra-renal artery at a rate of 0.04ml/min for 40 minutes. The same experiments were conducted in GRK4 A142V and GRK4 Wild Type transgenic mice. The ETBR function were also checked in the wild-type and A142V transfected renal proximal tubule (RPT) cells from mice.
Results: We found that diuresis and natriuresis of ETBR agonist, BQ3020, in Wistar-Kyoto (WKY) rats, which was impaired in SHRs. The GRK4 expression was higher in renal cortex from SHRs as compared with WKY rats. In GRK4 A142V transgenic mice, it resulted that ETBR-mediated diuresis and natriuresis was impaired compared with Wild type. In wild-type transfected cells, activation of ETBR inhibited Na+-K+-ATPase activity; while in A142V transfected cells, the inhibitory effect was lost. There are co-localization and co-immunoprecipitation between ETBR and GRK4 in RPT cells. The linkage of ETBR/GRK4 was higher in wild-type cells than in A142V cells. Similar phenomenon was found in the kidney from WKY and SHRs, SHRs had higher ETBR/GRK4 linkage, accompanied with higher ETBR phosphorylation, which might account for the impaired ETBR function in hypertension.
Conclusions: This study provides a mechanism by which GRK4, via regulation of renal ETBR function, participates in the pathogenesis of hypertension.

GW25-e1095

Cardiac Electrical Activity Improved by Overexpression of the Sarcoplasmic Reticulum Ca^{2+}-ATPase in Rat Myocardial Failure After Myocardial Infarction Evaluated by Microelectrode Arrays Technology

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Objectives: To explore overexpression recombinant adenovirus (rAd) -mediated sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA2a) for cardiac rhythmicity and conductivity in rat heart failure after myocardial infarction and its possibly electrical mechanisms.
Methods: 26 adult male SD rats were randomly divided into three groups: sham group (n=10), rAd.β-gal group (n=8) and rAd.SERCA2a group (n=8). Sham operation consisting of thoracotomy and cardiac exposure but without coronary artery ligation. RAd.β-gal group and rAd.SERCA2a group were ligated the left anterior descending coronary artery for rat heart failure animal model after myocardial infarction, while transfecting β-gal and SERCA2a gene into heart respectively. We used ultrasound electrocardiogram for evaluating cardiac diastolic and systolic function, ECG monitoring and microelectrode arrays (MEA) technology for myocardium electrical activity in vitro.
Results: rAd carrying SERCA2a and β-gal gene were successfully transfected in heart failure rats. rAd.SERCA2a group could improve failing heart function, the ventricular end diastolic volume, left ventricular end-systolic volume, left ventricular ejection fraction and fractional shortening. Compared with the sham group, ECG could be found that QT interval prolonged (94.7 ms$\pm$1.55 ms.vs.111.02 ms$\pm$7.42 ms, n=6, $P<0.05$) and the incidence rate of premature ventricular contractions (PVC) was 71.5% in rAd.B-gal group, but in rAd.SERCA2a group QT interval shortened and the incidence rate of PVC was 14.3%. No significant difference in the heart rate of rAd.SERCA2a group by MEA records. However, compared with the rAd.β-gal group, the maximum field potential, the minimum field potential and field potential duration were prolonged (0.64 mV$\pm$0.13 mV. vs. 0.82 mV$\pm$0.39 mV, 1.35 mV$\pm$0.12 mV. vs. 1.88 mV$\pm$0.57 mV, 113.23 ms$\pm$12.02 ms. vs. 124.17 ms$\pm$21.08 ms, respectively, n=6, $P<0.05$) in rAd.SERCA2a group. The field potential duration were statistically different between the infarct zone and the contralateral normal zone (60.36 ms$\pm$2.08 ms. vs. 103.24 ms$\pm$7.35 ms, n=5, $P<0.05$) in rAd.β-gal group, and field potential duration dispersion in infarct zone with 60 channels record was larger than rAd.SERCA2a group. The conduction time was simultaneous in rAd.SERCA2a group, and the cardiac electro-conduction activity could keep consistency and improve in myocardial infarction tissue.
Conclusions: Overexpression of SERCA2a may significantly improve left ventricular systolic and diastolic function, as well as it may be reduced incidence of arrhythmias in heart failure model after myocardial infarction and improve uniform conduction of cardiac electrical activity. MEA technology is an ideal technology for observing rhythm, frequency and conduction activities in cardiovascular disease animal models.

GW25-e1111

Anti-inflammatory Effects of Tanshinone IIA on Oxidative-injured Vascular Endothelial Cells are Mediated by Estrogen Receptor Activation and Through ERK Signaling Pathway

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Objectives: To investigate the estrogenic protective effect and mechanism of Tanshinone IIA on oxidative-injured vascular endothelial cells.